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EXAMINER	
UNGAR, SUSAN NMN	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,041	REED ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *18 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19,34 and 60-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19, 34, 60-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed December 1, 2003 in response to the Office Action of June 2, 2003 is acknowledged and has been entered. The Communication in Response to Notice of Non-Compliant Amendment filed March 18, 2004 in response to the Office Action mailed February 18, 2004 is acknowledged and has been entered. Previously pending claims 19 and 34 have been amended and claims 60-74 have been added. Claims 19, 34, 60-74 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. Claims 19 and 34 remain rejected and newly added claims 60-74 are rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action mailed June 2, 2003, pages 10-14 and pages 17-23.

Applicant argues that (a) the specification provides enablement for the full scope of the claims and that an effective agent obtained using the method of the invention need not be used for *in vivo* treatment of disease and that (b) claims 19 and 34, as amended are directed to a method of identifying an effective agent that alters the association of CAP-1 with CD40 or a polypeptide that contains a TRAF domain, (c) the specification teaches the structural characteristics of a polypeptide containing a TRAF domain and reiterates teachings of the specification in Figure 3 and page 16, (d) the specification provides those skilled in the art with guidance for preparing a CAP-1 for use in the claimed methods wherein the specification provides the amino acid sequencer of human CAP-1 and methods of making said CAP-1, (e) the specification

teaches a variety of assays for determining that an agent alters association of CAP-1 with a second polypeptide, (f) the teaching in the specification of the percent identity between CAP-1, TRAF1 and TRAF2 is sufficient for one skilled in the art to recognize that CAP-1 indeed contains a TRAF domain, and the teaching of the specification that TRAF domains in general are capable of homodimerization and heterodimerization would have led one skilled in the art to understand that the TRAF domain of CAP-1 can associate with TRAF domains of other polypeptides, with the TRAF domains of TRAF1 and TRAF2 being exemplary.

The arguments have been considered but have not been found persuasive because (a') although the specification teaches that the term "effective agent" is used to mean an agent that can alter the association of a CAP with a second molecule or alter the activity of a CAP, the specification also teaches that an effective agent can also be useful as a medicament to treat pathology characterized by an abnormal cell function (p. 22, lines 3-20). Given the wording of the claims, that is that they are drawn to a "method of identifying an effective agent that alters the association of Cap-1 with a second polypeptide", it is clear from the construction of the claim and the teaching of the specification that the "effective agent" is intended to include not only an agent that alters the association of Cap-1 with a second polypeptide, but is also drawn to the identification of a medicament and the specification clearly contemplates the use of the medicament, *in vivo*, for the effective treatment of disease, (b') as amended the claims are not limited to method of identifying an effective agent that alters the association of CAP-1 with CD40 or a polypeptide that contains a TRAF domain, the claims as written are broadly and reasonably read to read on an effective agent which

alters the association, but is not limited to *in vitro* effectivity as clearly disclosed in the specification, (c') the issue raised here is not that the specification does not teach structural characteristics of a polypeptide containing a TRAF domain, but rather that the information in the specification does not enable any person skilled in the art to which it pertains to practice the invention with a second molecule other than CAP-1 and CD40 and the teachings for how to assess TRAF domain dimerization do not provide enablement. Although Applicant insists that the teaching of the specification enables the claims, in support of Examiner's argument and purely in answer to Applicant's arguments it is noted that Whirter et al (Cold Spring Harbor Symposia on Quantitative Biology, 1999, 64:551-562) specifically teach that although CAP-1 (which has been renamed TRAF-3) heterodimerizes with TRAF5, both sequences contain 4.5 heptads proximal to the TRAF-C domain with two homologous core histidines. In both sequences this segment is preceded by a stutter in the sequence register, two additional heptads and complementary gaps in sequence alignment. These features, which are unique to TRAF3 and TRAF5would be expected to block association with the other TRAFs. Formation of the TRAF3/5 complex also may require the unique isoleucine zipper domains amino-terminal to the TRAF-N domain (para bridging columns 1 and 2 of page 554). It appears that although Applicant insists that the specification provides adequate enablement for the dimerization of TRAF-3 with TRAF 1 and TRAF2, that this dimerization would not be expected to take place by those of ordinary skill in the art given the teachings of Whirter et al, (d') although the specification provides guidance for preparing a CAP-1, the specification does not enable the claimed invention for the reasons of record,(e') it is clear from the teachings

of Whirter et al that the specification does not enable the claimed invention, (f') given the teachings in the art, it does not appear that it is possible for CAP-1 to associate with the exemplary TRAF1 and TRAF2. Now does it appear that it would be possible for TRAF3 to associate with any TRAF domain other than TRAF5 Applicant's arguments have been considered but have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 19, 34, 60-62 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 19, 34, 60-62 are drawn to a method of identifying an effective agent that alters the association of CAP-1 with a second peptide, wherein said second peptide is a polypeptide containing a TRAF domain. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus

> because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such

characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of a polypeptide containing a TRAF domain which binds to CAP-1, per Lilly by structurally describing a representative number of polypeptides containing a TRAF domain which bind to CAP-1 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe polypeptides containing a TRAF domain which binds to CAP-1 required to practice the methods of the claims in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of polypeptides containing a TRAF domain that binds to CAP-1, nor does the specification provide any partial structure of such polypeptides, nor any physical or chemical characteristics of said polypeptides nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses TRAF 1 and 2 with

limited homology to SEQ ID NO:2, this does not provide a description of polypeptide containing a TRAF domain which binds to CAP-1 would satisfy the standard set out in Enzo.

The specification also fails to describe the polypeptide containing a TRAF domain which binds to CAP-1 by the test set out in Lilly. The specification describes only discloses TRAF 1 and 2 with limited homology to SEQ ID NO:2, this does not provide a description of a polypeptide containing a TRAF domain which binds to CAP-1 . Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the polypeptide containing a TRAF domain which binds to CAP-1 that is required to practice the claimed invention. Since the specification fails to adequately describe the polypeptide containing a TRAF domain which binds to CAP-1, it also fails to adequately describe the method of identifying an effective agent that alters the association of CAP-1 with a polypeptide containing a TRAF domain which binds to CAP-1 .

Applicant's arguments drawn to the rejection of claims 19 and 34 under the written description provisions of 35 USC 112, first paragraph are relevant to the instant rejection.

Applicant argues that the specification provides adequate description for the full scope of the invention as now claimed and one skilled in the art would recognize that

Applicants were in possession of a genus of polypeptides containing TRAF domains capable of associating with CAP-1 and that to show possession of a claimed genus, all that is required is to show that Applicant was in possession of the necessary common attributes. Further Applicant argues that the specification provides sufficient explicit description of a TRAF domain and exemplify several TRAF domain containing polypeptides that can be used in the claimed methods. Applicant then reiterates the teaching in the specification drawn to TRAF domain containing polypeptides useful in the invention. The arguments have been considered but have not been found persuasive, the claims as newly amended are not drawn to TRAF-1 or TRAF-2 but are drawn to polypeptides containing TRAF domains, for the reasons set forth above, Applicant has not provided an adequate description of the full scope of the invention and the teachings drawn to TRAF-1 and TRAF-2 are not sufficient to provide a representative number of species or to provide common elements to demonstrate that Applicant's were in possession of a genus of polypeptides containing TRAF domains capable of associating with CAP-1.

6. If Applicant were to be able to overcome the rejections set forth above, Claims 19, 34, 60-62 would still be rejected under 35 USC 112, first paragraph because the specification while enabling for a method of identifying an effective agent that alters the association of CAP-1 with CD40 does not reasonably provide enablement for a method if identifying an effective agent that alters the association of CAP-1 with a polypeptide containing a TRAF domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims

Applicant's submission of evidence correlating CAP-1 to TRAF3 is noted. In particular, the COPE Cytokines Online Pathfinder Encyclopedia provides evidence that CAP-1 has been renamed TRAF3.

The claims are drawn to a method of identifying an effective agent that alters the association of CAP-1 with a polypeptide containing a TRAF domain. This means any polypeptide containing a TRAF domain. The specification teaches that, because of a 57% and 59% amino acid identity between the C terminal TRAF domains of TRAP 1 and TRAF2 respectively and the cytosolic domain of CAP-1, the cytosolic domain of CAP-1 is referred to as a TRAF domain (p. 54, lines 6-22). The cytoplasmic TRAF domain of CAP-1 can bind to CD40 and can form homodimers. The TRAF1 and TRAF2 proteins can form homotypic and heterotypic dimers, suggesting that their TRAF domains mediate dimer formation in a manner similar to the TRAF domain of CAP-1. In view of the structural similarities between the TRAF domains of TRAF1, TRAF2 and CAP-1, it is likely that all three proteins can form dimers with each other in a cell (p. 16, lines 5-16). One cannot extrapolate the teaching of the specification to the scope of the claims because, assuming for examination purposes that TRAF3 is indeed CAP-1, it was well known in the art at the time the invention was made that TRAF3 does not form heterodimers with either TRAF1 or TRAF2. In particular, Whirter et al (Cold Spring Harbor Symposia on Quantitative Biology, , 1999, 64:551-562), in agreement with the specification teaches that TRAF1 and TRAF 2 form heterodimers (p. 553, col 2, last paragraph). On the other hand the reference specifically teaches that although TRAF3 heterodimerizes with TRAF5, both sequences contain 4.5 heptads proximal to the TRAF-C domain

with two homologous core histidines. In both sequences this segment is preceded by a stutter in the sequence register, two additional heptads and complementary gaps in sequence alignment. These features, which are unique to TRAF3 and TRAF5, would be expected to block association with the other TRAFs. Formation of the TRAF3/5 complex also may require the unique isoleucine zipper domains amino-terminal to the TRAF-N domain (para bridging columns 1 and 2 of page 554). Given the above, no one of ordinary skill in the art would believe the specification's hypothesized heterodimer formation between CAP-1, TRAF1 and TRAF2 in the absence of objective experimental evidence demonstrating that heterodimerization. Further, as drawn to other TRAF polypeptides, Whirter et al specifically teach that there are TRAFs that fail to hetero-oligomerize and that they do this because they contain TRAF-N domain sequences that are mismatched in length, polarity and charge. Given the above, it cannot be predicted whether, or which polypeptides containing TRAF domains would function as claimed. It is noted in the interests of compact prosecution and for Applicant's convenience that amendment of the claims to recite TRAF5 as the "second polypeptide" would result in a rejection under 35 USC 112, first paragraph "New Matter" because TRAF5 is neither disclosed nor contemplated in the specification as originally filed. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

7. Claims 60-61, 64-65, 68-69, 72-73 are rejected under 35 USC 112, first paragraph as the specification does not contain a written description of the claimed invention. The limitation of a CAP-1 wherein said CAP-1 comprises amino acids 384-540/53-91 of SEQ ID NO:2 has no clear support in the specification and the claims as originally filed. Although Applicant argues support for the newly added limitations in claims cancelled in the instant Application a review of the cancelled claims did not reveal support for the newly claimed limitations. It is suggested that Applicant review the cancelled claims in the instant application. Further, in the interests of compact prosecution, Examiner will consider the pages referred to in the arguments on pages 7-8 of the response. Applicant argues that support for the newly claimed limitation drawn to amino acids 384-540 is provided in the specification on page 55, lines 18-23 and that support for the newly claimed limitations drawn to amino acids 53-91 is provided in the specification on page 54, lines 24-26. The argument has been considered but has not been found persuasive. A review of the suggested support for the amino acid range of 384-540 of SEQ ID NO:2 reveals support for the essential conserved region between CAP-1 and TRAF1 and TRAF2 is represented by positions 385-536 but no support for a method of identifying an effective agent that alters the association of CAP-1 wherein said CAP-1 comprises amino acids 384-540 of SEQ ID NO:2 which reads on polypeptides consisting of the claimed amino acid range as well undefined polypeptides comprising said range of SEQ ID NO:2. The specification does not contemplate the use of the broadly claimed polypeptides in the method as claimed. In addition, the sequences recited in the specification are not limited to SEQ ID NO:2. Indeed, SEQ ID NO:2 is not the only

CAP-1 disclosed in the specification wherein it is taught that human CAP-1 includes amino acid sequences similar to SEQ ID NO:2 but having one or more amino acid additions, deletions or substitutions that do not substantially alter the ability of the encoded protein to function like CAP-1 (p. 14, lines 1-15). Further, the suggested support is not drawn to the range recited in the claims. In addition, a review of the suggested support for the amino acid range of 53-91 reveals support for the CAP-1 containing a RING finger domain consensus sequence like TRAF2 but no support for a method of identifying an effective agent that alters the association of CAP-1 wherein said CAP-1 comprises amino acids 53-91 of SEQ ID NO:2 which reads on polypeptides consisting of the claimed amino acid range as well undefined polypeptides comprising said range of SEQ ID NO:2. As noted above, the sequences recited in the specification are not limited to SEQ ID NO:2. Indeed, SEQ ID NO:2 is not the only CAP-1 disclosed in the specification wherein it is taught that human CAP-1 includes amino acid sequences similar to SEQ ID NO:2 but having one or more amino acid additions, deletions or substitutions that do not substantially alter the ability of the encoded protein to function like CAP-1 (p. 14, lines 1-15). The subject matter claimed in claims 60-61, 64-65, 68-69, 72-73 broadens the scope of the invention as originally disclosed in the specification.

8. If Applicant were able to overcome the rejections set forth above, Claims 19, 34, 60-61, 63-65, 67-70, 71-73 would still be rejected under 35 USC 112, first paragraph because the specification, while enabled for a method of identifying an effective agent that alters the association of CAP-1, SEQ ID NO:2, with a second polypeptide does not reasonably provide enablement for a method of identifying an

effective agent that alters the association of CAP-1 with a second polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to a method of identifying an effective agent that alters the association of CAP-1 with a second polypeptide. This means any CAP-1 as defined by the specification. The specification teaches the invention provides human CAP-1 having substantially the amino acid sequence shown in SEQ ID NO:2 wherein "substantially the amino acid sequence" means not only SEQ ID NO:2 but also amino acid sequences that are similar to SEQ ID NO:2 but have one or more amino acid additions, deletions or substitutions that do not substantially altered the ability of the encoded protein to function like CAP-1 and bind to CD40 or to another protein such as a member of the TRAF family of proteins. It is noted that this definition of human CAP-1 is clearly applicable to claims 60-61, 64-65, 68-69, 72-73 which recite CAP-1 polypeptides comprising defined ranges of SEQ ID NO:2. The specification further teaches that the invention provides a substantially purified human CAP-1 (p. 3, line 16) and teaches the amino acid sequence of CAP-1, SEQ ID NO:2 (p. 4, lines 5-10) wherein the invention provides a novel CD40 associated protein designated CAP-1 (p. 5, lines 4-5). The specification teaches that CAP-1 was isolated from a human B cell cDNA library wherein two clones contained identical cDNA inserts suggesting that the two clones arose as library-amplified copies of a single cDNA. The cDNA was named CAP-1 for CD40 associated protein-1 (p. 46, lines 4-15). The specification further teaches that fusion proteins were produced and *in vitro* binding between CAP-

1 and CD40 was demonstrated (p.48, lines 23-24). The specification further teaches that a cDNA library can be screened to identify a new CAP (p. 51, lines 1-5). The complete CAP-1 ORF encodes a 543 amino-acid protein (p. 53, lines 21-35).

One cannot extrapolate the teaching of the specification to the scope of the claims because the human CAP-1 defined in the specification clearly encompasses polypeptides with additions, deletions or substitutions that do not substantially altered the ability of the encoded protein to function like CAP-1 and bind to CD40 or to another protein such as a member of the TRAF family of proteins, however, Applicant has not enabled all of these types of modified polypeptides.

In particular, protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Bowie et al, of record, teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single

amino acid in a sequence are exemplified by Burgess et al, of record, who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al, of record who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. It is clear that the effect of undefined and unlimited additions, substitutions, deletions of amino acid residues on the binding function of SEQ ID NO:2 cannot be predicted. The specification does not provide any information or guidance drawn to which amino acid residues can be deleted, substituted or added such that the encoded protein will function like CAP-1 and bind to CD40 or to another protein such as a member of the TRAF family of proteins. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and it cannot be predicted how to make the claimed CAP-1 so that the method will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. Claims 19, 34, 60-61, 63-65, 67-70, 71-73 are rejected under 35 USC 112, first paragraph as the instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one

skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claims are drawn to methods of identifying an effective agent that alters the association of CAP-1 with a second polypeptide, wherein CAP-1 comprises amino acids 384-540 of SEQ ID NO:2, amino acids 53-91 of SEQ ID NO:2.

The specification discloses SEQ ID NO:2. The claims, as written, however, encompass polypeptides which vary substantially in length and also in amino acid composition given the definition of human CAP-1 recited in the specification. In particular, the specification teaches that the invention provides human CAP-1 having substantially the amino acid sequence shown in SEQ ID NO:2 wherein "substantially the amino acid sequence" means not only SEQ ID NO:2 but also amino acid sequences that are similar to SEQ ID NO:2 but have one or more amino acid additions, deletions or substitutions that do not substantially altered the ability of the encoded protein to function like CAP-1 and bind to CD40 or to another protein such as a member of the TRAF family of proteins. It is noted that the term "substantially" as drawn to polypeptide function is not defined by the specification. Given the above, it is clear that the claims are drawn to a whole universe of polypeptides that differ in length and amino acid composition and ability to function like CAP-1.

The instant disclosure of a single species of amino acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. Although drawn to the DNA arts, the findings in *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) are relevant to the instant rejection. It was found that a description of a

genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed and no identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a single CAP-1 sequence is insufficient to describe the genus. One of skill in the art would reasonably conclude that the Applicant did not have possession of the claimed invention at the time of filing and that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Therefore only an isolated CAP-1, SEQ ID NO:2 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

10. If Applicant were able to overcome the rejections set forth above, Claims 19, 34, 60-74 would still be rejected under 35 USC 112, first paragraph because the specification, while enabled for a method of identifying an effective agent that inhibits/decreases the binding/association of CAP-1 with a second polypeptide does not reasonably provide enablement for a method of identifying an effective agent that alters the association of CAP-1 with a second polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of identifying an effective agent that alters the association of CAP-1 with a second polypeptide. This means an effective agent that increases or decreases the association of CAP-1 with a second polypeptide. The specification teaches that the association of CAP-1 with CD40 in a cell can be altered due to the expression in the cell of a variant CAP-1 or variant CD40, either of which can compete for binding with CAP-1 that normally binds to CD40 in the cell. (Thus, it appears that the association contemplated is the binding of CAP-1 to a second polypeptide.) In this case, the association of CAP-1 with CD40 can be decreased in a cell (p. 11, lines 4-15). One cannot extrapolate the teaching of the specification to the scope of the claims because the specification does not provide either guidance or information on any association between CAP-1 and any other polypeptide, except binding. Although the specification clearly delineates agents that would interfere with that binding, no agents are taught that would increase the binding of CAP-1 to a second polypeptide, indeed there is no disclosure of what "increased" association encompasses. Is it tighter binding, quicker binding? The specification provides no

suggestion as to what this might be and provides no guidance as to assays for determining whether the association has increased. Further, the specification provides no guidance as to a source for such agents to be assayed, and given that there appears to be only one CAP-1 binding site for CD40, if binding is not tighter or quicker, it is unclear, once the site is filled how any agent would increase the binding of a second polypeptide to CAP-1. No examples of any agents that increase binding in any protein model which could provide guidance to one of ordinary skill are disclosed. The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that an effective agent that increases the association of CAP-1 could be identified by the invention as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

11. Claims 67-70 are rejected under 35 USC 112, second paragraph because although the claims are drawn to a method for identifying an effective agent that alters the association of CAP-1 with CD40 in a test sample, the claims are missing an essential element, that is, that the test sample comprises CAP-1 and CD40.

12. Claims 19, 34 and 60-74 are rejected under 35 USC 112, second paragraph because the claims are confusing in the recitation of the phrase "an effective agent that alters the association of CAP-1 with a second polypeptide". The claims are confusing given the clear definition in the specification that an effective agent is not only one that alters the association of CAP-1 with a second polypeptide but also states that an effective agent is one that is useful as a medicament for the treatment of disease.

Applicant's arguments drawn to the rejection of claims 19 and 34 under 35 USC 112, second paragraph in the previous action are relevant to the instant rejection. Applicant argues that the claims have been amended to recited that an effect agent "alters the association of CAP-1 with a second polypeptide". However, a review of the claim language reveals that the claims are not limited to that effect and given the teaching in the specification, the claims as written read on the "effective agent" as a medicament. The rejection can be obviated by amending the claims to recite, for example, a method of identifying an agent effective to alter the association of Cap-1 with a second polypeptide.

13. Claims 19, 34, 60-61, 63-65, 67-69, 71-73 are rejected under 35 USC 112, second paragraph because the claims recite CAP-1 as the sole means of identifying the claimed polypeptide. The use of laboratory designations only to identify a particular polypeptide renders the claims indefinite because different laboratories may use the same laboratory designations to define completely polypeptides. Amendment of the claims to include a sequence identified will overcome the instant rejection because sequence identification numbers are unique identifiers which unambiguously define a given polypeptide.

14. All other objections and rejections recited in paper mailed June 2, 2003 are hereby withdrawn.

15. No claims allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from

7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571-272-0841. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 872-9306.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
June 3, 2004